REMARKS

Claims 1 – 59 were pending. Claims 1, 2, 14 – 24, 27 – 29, and 31 - 50 have been cancelled. Claims 51 – 61 have been withdrawn. Claims 3 – 13 and 25 have been amended. New claim 62 has been added. No new matter has been added by virtue of the amendments, support being found throughout the specification and the claims as originally filed. In particular, support for the amendments can be found at pages 15 – 16 and in Example 5 on page 29.

Any cancellation of the claims was done solely to expedite the prosecution of the application. Applicant reserves the right to pursue the claims as originally filed in this or a separate application(s).

As the elected invention is now drawn to a probe set, the Examiner has withdrawn the restriction among the particular probes in view of the cancellation of the claims. (Office Action, p.2).

Claim Rejections

35 U.S.C. §112, first paragraph

Claims 3 – 13, 25, 26 and 30 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants respectfully disagree.

Present claim 25 recites a PNA probe set comprising a PNA probe that is at least 95% homologous to SEQ ID NO: 6, a PNA probe that is at least 95% homologous to SEQ ID NO: 7 and a PNA probe that is at least 95% homologous to SEQ ID NO: 8.

The Examiner argues that the claims "recite that the PNA probes are at least 86% identical to SEQ ID NOs: 6, 7 and 8 (and) the specification teaches at pages 15 – 16 that 'the probing nucleobase sequence may be only as much as 86% homologous to the probing nucleobase sequences identified above." (Office Action, p.3). The Examiner argues that "this does not provide conception for the recitation of 'at least

86% identical' to the probe set because the concept of homology and identity are not the same.

Without acquiescing to the validity of the foregoing rejection, and only in the interest of advancing prosecution and allowance of the claims, Applicants have amended the present claims to recite a PNA probe that is at least 95% homologous to SEQ ID NO: 6, a PNA probe that is at least 95% homologous to SEQ ID NO: 7 and a PNA probe that is at least 95% homologous to SEQ ID NO: 8.

Accordingly, Applicants respectfully request that the foregoing rejection be withdrawn.

Claims 3 – 13, 25, 26 and 30 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. Applicants respectfully disagree.

The present claims have been set forth above.

The Examiner argues that "(t)he specification does not teach variants of SEQ ID NOS: 6, 7 or 8 (and) the specification does not teach the 'target sequence' in genome or nucleobase sequence of the microorganism such that the skilled artisan would be able to readily envision other PNA probes for targeting." (Office Action, p.4).

Without acquiescing to the validity of the foregoing rejection, and only in the interest of advancing prosecution and allowance of the claims, Applicants have amended the present claims to recite a PNA probe that is at least 95% homologous to SEQ ID NO: 6, a PNA probe that is at least 95% homologous to SEQ ID NO: 7 and a PNA probe that is at least 95% homologous to SEQ ID NO: 8. Further, Applicants teach in the specification, for example at page 15, line 26, that "a substantially complementary probing nucleobase sequence might be used since it has been demonstrated that greater sequence discrimination can be obtained when utilizing probes wherein there exists one or more point mutations (base mismatch) between the probe and the target sequence (See: Guo et al., Nature Biotechnology 15:331-335 (1997))." Accordingly, one of skill in the art could readily envisage variants that are useful for detection.

Applicants respectfully request that the rejection be withdrawn.

35 U.S.C. §112, second paragraph

Claims 3 – 13, 25, 26 and 30 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully disagree.

The present claims have been set forth above.

The Examiner argues that "(a)s to claim 25 and all dependent claims, it is unclear from the claim construction how may probes must be present in the probe set, at least three?." (Office Action, p.6). Claim 25 has been amended to recite the phrase "at least three."

The Examiner argues that "(a)s to claim 3, the term "the Staphylococcus probe" is indefinite inasmuch as it lacks antecedent basis in the independent claim 25. (Office Action, p.6). Claim 3 has been amended to recite proper antecedent basis.

The Examiner argues that "(a)s to claims 3 – 13, the claims are prima facie indefinite as the term 'the PNA probe of claim 25,' lacks clear and unambiguous support in the independent claim 25 from which they depend." Claims 3 – 13 have been amended to recite a probe set.

The Examiner argues that "as to claims 3 – 13, the claims are also confusing in that the claims are also confusing in that the claims recite 'a target sequence' and the specification teaches that the target sequence is a nucleobase sequence and the claims do not recite a nucleobase sequence." (Office Action, p.7). Applicants disagree. Applicants clearly describe PNA probes of the invention, for example, beginning at page 14, line 30. Applicants teach that:

> The probing nucleobase sequence of a probe of this invention is the specific sequence recognition portion of the construct. Therefore, the probing nucleobase sequence is a nucleobase sequence designed to hybridize to a specific target sequence wherein the presence, absence or amount

> of the target sequence can be used to directly or indirectly detect the presence, absence or number of organisms of interest in a sample. Consequently, with due consideration to the requirements of a probe for the assay format chosen, the length and sequence composition of the probing nucleobase sequence of the probe will generally be chosen such that a stable complex is formed with the target sequence under suitable hybridization conditions

Applicants teach preferred PNA probes, including SEQ ID NOs 6, 7 and 8, for analysis of Staphylococcus species (see, e.g. p.15, line 8).

Accordingly, Applicants respectfully request that the foregoing rejections be withdrawn.

35 U.S.C. §103(a)

Claims 3 – 13, 25, 26 and 30 are rejected under 35 U.S.C. §103(a) as being unpatentable over Hashida et al. (WO 03/106676) in view of Ray et al. (FASEB Journal, 14: 1041 – 1060, 2000). Applicants respectfully disagree.

The Examiner argues that Hashida et al. teach probe sets for the detection and identification of *S. hominis* (SEQ ID NOs 43, 44 and 45), *S. warneri* (SEQ ID NOs: 46, 47 and 48), *S. haemolyticus* (SEQ ID NOs 49, 50 and 51), *S. epidermidis* (SEQ ID NOs: 57, 58 and 59), *S. aureus* (SEQ ID NOs: 96, 97 and 98) and *S. saprophyticus* (SEQ ID NOs: 122, 123 and 124). (Office Action, p.8). The Examiner argues that "Hashida et al. teach probe sets for use in the identification of microorganisms...(and) that SEQ ID NOs: 43 and 57 are 100% identical as compared to SEQ ID NO: 6...that SEQ ID NO: 46 is 100% identical as compared to SEQ ID NO: 7...that SEQ ID NO: 49 is 100% identical as compared to SEQ ID NO: 8." (Office Action, p.8). The Examiner contends that "Hashida et al. differ by not teaching PNA probes corresponding to the nucleobases (but) Ray et al. teach that peptide nucleic acid probes are chemically stable and resistant to hydrolytic (degradation) (and)...despite the backbone variations from natural nucleic acids, PNA is still capable of sequence-specific binding to DNA as well as RNA." (Office Action, p.8). The Examiner argues that "(i)t would have been

prima facie obvious to make PNA probes corresponding to the *Staphylococcus* probe sequences of Hashida et al. and combine the probes for all the *Staphylococcus* spps in a probe set...to discriminate among the *Staphylococcus* spp for diagnostic and detection purposes." (Office Action, p.9). Applicants disagree.

As described in the specification, DNA probes for analysis of *Staphylococcus aureus* and all *Staphylococcus* species (genus-specific probes) have been previously described, as well as PNA probes for the analysis of *S. aureus*. **These probes all target sequences that are either species- specific or genus-specific**. (page 2, lines 15 – 20, emphasis added). Further, as stated in the specification, the design of probes targeting **a cohort of species** is particularly problematic and requires a combination of highly specific probe constructs and unique target sequences. (p.2, lines 32 – 34, emphasis added). Simultaneous analysis of both S. aureus and other Staphylococcus species would be advantageous as treatment decisions for the presence of either S. aureus or other Staphylococcus species would be based on a positive test results. This feature would also offer a considerable advantage when a mixture of S. aureus and other Staphylococcus species are present. Accordingly, the present invention is directed to a PNA probe set comprising a PNA probe that is at least 95% homologous to SEQ ID NO: 6, a PNA probe that is at least 95% homologous to SEQ ID NO: 7 and a PNA probe that is at least 95% homologous to SEQ ID NO: 8. Applicants teach in Example 5 that all of the probes are directed towards a phylogenetically conserved region of rRNA target sequence that varies slightly between Staphylococcus species. (p. 29, lines 5 – 7). Referring to Table 5 on page 29, Applicants show that the none of the probes tested result in detection of *S.aureus* (red fluorescent signal), and all of the species described in rows C through G of the Table (*S. aureus, S. epidermidis, S. hominis, S. haemolyticus, S. lugdenensis, S. sarophyticus*) are detected (display red fluorescence) when detected with the probe set comprising SEQ ID NO: 6, SEQ ID NO: 7 and SEQ ID NO: 8. (see, e.g. Table 5 and p. 29, lines 15 – 24). Accordingly, Applicants teach that "a probe mixture can be made which detects a cohort of species by one fluorescent label, and a single species with a second fluorescent label." (p.31, lines 13 – 15).

The Hashida reference, as pointed out by the Examiner, teaches probe sets for the detection of S. hominis. The Examiner argues Hashida et al. teaches that SEQ ID NOs 43, 44 and 45 are a probe set for the detection and identification of *S.hominis*. (Office Action, p.8). The Examiner argues Hashida et al. teaches that SEQ ID NOs 46, 47 and 48 are a probe set for the detection and identification of *S.warneri*. (Office Action, p.8). The Examiner argues Hashida et al. teaches that SEQ ID NOs 49, 50 and 51 are a probe set for the detection and identification of *S. haemolyticus*. (Office Action, p.8). The Examiner argues Hashida et al. teaches that SEQ ID NOs 57, 58 and 59 are a probe set for the detection and identification of *S. epidermidis*. (Office Action, p.8). The Examiner argues Hashida et al. teaches that SEQ ID NOs 122, 123 and 124 are a probe set for the detection and identification of *S. saphrophyticus*. (Office Action, p.8). Accordingly, Hashida teaches **probes sets that all target sequences that are species- specific**. As pointed out above, the present invention has particularly designed probes to target a cohort of species. Nowhere does the Hashida et al. reference teach or suggest picking out the particular probes that correspond to a probe set comprising SEQ ID NO: 6, SEQ ID NO: 7 and SEQ ID NO: 8. Nowhere does the Hashida et al. reference teach or suggest any probe set comprising SEQ ID NO: 6, SEQ ID NO: 7 and SEQ ID NO: 8 that can detect a cohort of species by one fluorescent label.

The Ray reference does not cure the defects of the Hashida reference. The Ray et al. reference merely provides background on the PNA and its potential use in medial and biotechnical applications. None of the cited references, alone or together, teaches or suggests any probe set comprising a PNA probe that is at least 95% homologous to SEQ ID NO: 6, a PNA probe that is at least 95% homologous to SEQ ID NO: 7 and a PNA probe that is at least 95% homologous to SEQ ID NO: 8, as claimed.

Applicants respectfully request that the rejection be withdrawn.

CONCLUSION

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Order No. 60218(48497).

Dated: March 8, 2010

Respectfully submitted,

By:

Customer Number 21874

Jonathan M. Sparks, Ph.D.
Registration No.: 53,624
EDWARDS ANGELL PALMER & DODGE LLP
P.O. Box 55874
Boston, Massachusetts 02205
(617) 517-5543
Attorneys/Agents For Applicant